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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,684	11/08/2001	Aristo Vojdani	IMSCI2.005A	9590

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EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,684	VOJDANI, ARISTO	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/15/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 18, 2005 has been entered.

2. Applicant's amendment of claim 1 is acknowledged and has been entered.

3. Claims 1-12 are currently pending.

Information Disclosure Statement

4. The copending application 10/004,929 in the information disclosure statement (IDS) submitted on November 15, 2004 has been considered but not entered as the application is not currently available to the public as a Pgpublication.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 2, 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 2 recites the limitation "the autoantigen for autoimmune disease" in the first two lines. There is insufficient antecedent basis for this limitation in the claim.

8. Claim 12 recites the limitation "the autoantigen for cardiovascular disease" in the first two lines. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, applicant fails to teach the steps where the level of a first set of antibodies selected from the group consisting of myosin antibody, oxidized LDL, heat shock protein-60 antibody, and β-2 glycoprotein-1 antibody and a second set of antibodies selected from the group consisting of lupus peptides, arthritis peptides, platelet glycoprotein, and immune complexes are determined and compared with each other to distinguish the presence or possibility of either autoimmunity or autoimmune disease from the presence or possibility of autoimmune disease and cardiovascular disease. In particular, figure 6 does not disclose how platelet glycoprotein relates to the possibility or presence of cardiovascular disease or autoimmune disease. Therefore, it is unclear if higher than normal levels of platlet glycoproteins would indicate possible autoimmunity or possible cardiovascular disease and autoimmune disease. In addition, figure 6 also appears to require all 7 antibodies to be measured, in order to

distinguish between optimal conditions, possible autoimmunity, and possible cardiovascular and autoimmune disease.

11. Even then, applicant would only be able to determine the possibility or presence of the specific cardiovascular diseases for which the antigens are associated with. For example, higher than normal levels of myosin antibody would not necessarily suggest the presence or possibility of artherosclerosis, and normal levels of myosin antibody would not mean that there is no presence or possibility of cardiovascular disease and autoimmune disease.

12. Furthermore, while applicant provides data showing possible autoimmunity as well as data showing possible cardiovascular and autoimmune disease, applicant does not clearly disclose the steps of comparing the data to establish possible cardiovascular and autoimmune disease from possible autoimmune disease, or comparing the data to establish possible cardiovascular and autoimmune disease from possible autoimmunity.

For example, if there are not higher than normal levels of antibodies in the second set of antibodies, this would actually suggest the patient is in optimal condition, even though the first set may or may not have higher than normal levels of antibodies. In fact if the first set has higher than normal levels of antibodies, the results would actually conflict with each other, as one set would indicate possible cardiovascular and autoimmune disease, whereas the other set would indicate optimal conditions.

13. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for a method for detecting antibodies against certain antigens and for indicating the presence or possibility of autoimmune disease, does not reasonably provide enablement for a method for distinguishing possible autoimmune disease from possible

cardiovascular disease with autoimmune disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to make or use the invention commensurate in scope with these claims. The specification, according page 24, merely refers to fig. 6 for diagnosing possible autoimmunity, and data interpretation of antibody levels to human target antigens relating to the possible autoimmunity. Figure 6 fails to establish that higher than normal levels of platelet glycoprotein would indicate the presence or possibility of autoimmune disease and cardiovascular disease, while higher than normal levels of all antibodies associated with autoimmune disease but not platelet glycoprotein would indicate the presence or possibility of autoimmune disease, as in figure 6, as applicant has only performed studies on oxidized LDL, heat shock protein 60 antibody, B-2 glycoprotein-1 antibody, immune complexes, arthritis peptides, and lupus peptides. Therefore, applicant would only be enabled at best for these 7 antigens.

14. Even then, applicant would only be able to determine the possibility or presence of the specific cardiovascular diseases for which the antigens are associated with. For example, higher than normal levels of myosin antibody would not necessarily suggest the presence or possibility of artherosclerosis, and normal levels of myosin antibody would not mean that there is no presence or possibility of cardiovascular disease and autoimmune disease.

15. Furthermore, based on the data from figure 6, it would appear that the levels of all 8 antigens would have to be measured in order to be able to distinguish between the likelihood of autoimmune disease and the likelihood of cardiovascular disease with autoimmune disease. Applicants have only stated that "detection of above normal levels of saliva IgA antibody against the antigens listed in Figure 6 can help to diagnose possible autoimmunity" (pg. 0104).

For example, if there are not higher than normal levels of antibodies in the second set of antibodies, this would actually suggest the patient is in optimal condition, even though the first set may or may not have higher than normal levels of antibodies. In fact if the first set has higher than normal levels of antibodies, the results would actually conflict with each other, as one set would indicate possible cardiovascular and autoimmune disease, whereas the other set would indicate optimal conditions. Specifically, the data presented in Figure 6, which suggests that lack of higher than normal levels of immune complexes, lupus peptide antibodies, and arthritic peptide antibodies would suggest a lack of possible autoimmunity, which appears to contradict claim 1, which recites that higher than normal levels of antibodies in the first set but not the second set would indicate the presence or possibility of cardiovascular disease **AND autoimmune disease**.

16. According to Strongin (Strongin, Sensitivity, specificity, and predictive value of diagnostic tests: definitions and clinical applications, 1993, Laboratory Diagnosis of Viral Infections, p. 211-219), a number of characteristics need to be considered in the development of any suitable diagnostic assay. These characteristics include the sensitivity of the assay, the true-positive test rate, the false-negative test rate, the specificity, the true-negative test rate, the false positive test rate, the predictive value, the prevalence, the efficiency or percentage of all results that are true, and the accuracy of the recited diagnostic assay. However, none of these characteristics appear to have been considered.

Additional considerations must also be examined to enable the clinician to practice the invention, including assessment of when the maximum sensitivity, maximum specificity, and maximum efficiency are desired, how is the maximum sensitivity or specificity achieved, and

how is the predictive value maximized. An essential understanding of these factors is required to enable the skilled artisan to accurately use and interpret any given diagnostic test. Specifically, the specification fails to disclose what is meant by the possibility of autoimmune disease or by the possibility of cardiovascular disease with autoimmune disease. Specifically, it is unclear how statistically significant are the results of this method.

Response to Arguments

17. Applicant's arguments with respect to claims 1-12 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nelson Yang
Patent Examiner
Art Unit 1641

LONG V. LE
SUPERVISORY PATENT EXAMINER
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06/24/05